REMARKS

Priority

The basis for denying the priority claim is unclear. For example, the provisional application (U.S. Serial No. 60/269,840) to which this application claims benefit, discloses SEQ ID NO:2. Clarification is requested.

Double-patenting

The provisional double-patenting rejection is noted, but since no claims have been indicated as allowable, there is no action necessary at this time.

Rejection under §112, first paragraph

It is stated on Page 4 of the Office action that the phrase "elicits antibodies specific for BVH-P7 of S pyogenes" does "not appear to have explicit written description in the specification as filed." The examiner's allegation that "explicit" description is necessary is not a correct formulation of the written description requirement. To satisfy the written description requirement, the specification needs to convey possession of the claimed invention to the skilled worker. Explicit language is not required. According to MPEP 2163.02: "An objective standard for determining compliance with the written description requirement is, 'does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed.' *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989)." See also, *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 19 USPQ2d 1111 (Fed. Cir. 1991). The specification "need not describe the claimed subject matter in exactly the same terms as used in the claims." *All Dental Prodx LLC v. Advantage Dental Products Inc.*, 64 USPQ2d 1945 (Fed. Cir. 2002).

Clear support for the recited phrase is provided throughout the specification. For example:

> (d) a polynucleotide encoding a polypeptide **capable of generating antibodies having binding specificity for a polypeptide comprising a sequence chosen from: SEQ ID NO: 2** or fragments or analogs thereof;
> (e) a polynucleotide encoding an epitope bearing portion of a polypeptide comprising a sequence chosen from SEQ ID NO: 2 or fragments or analogs thereof;

Page 5, lines 26-32 (Emphasis added).

> d) a polynucleotide encoding a polypeptide **capable of raising antibodies having binding specificity for a polypeptide** comprising a sequence chosen from: SEQ ID NO: 2;
> e) a polynucleotide encoding an epitope bearing portion of a polypeptide comprising a sequence chosen from SEQ ID NO: 2

Page 6, lines 11-15 (Emphasis added).

> In addition to the DNA and RNA molecules, the invention includes the corresponding polypeptides and monospecific antibodies that specifically bind to such polypeptides. In a further embodiment, the polypeptides in accordance with the present invention are antigenic.
> In a further embodiment, the polypeptides in accordance with the present invention are immunogenic.
> In a further embodiment**, the polypeptides in accordance with the present invention can elicit an immune response** in a host.
> In a further embodiment, the present invention also relates to polypeptides which are able to raise **antibodies having binding specificity to the polypeptides of the present**

invention as defined above.

An antibody that "has binding specificity" is an antibody that recognizes and binds the selected polypeptide but which does not substantially recognize and bind other molecules in a sample, e.g., a biological sample.

Page 7, line 26-Page 8, line 12 (Emphasis added).

(iv) a method for inducing an immune response against Streptooccus

Page 14, lines 12-13.

Evaluation of the attachment of **BVH-P7-specific antibodies** at the surface of intact cells of S. pyogenes ATCC12384 strain (serotype M3)

Page 33, lines 15-18 (Emphasis added).

Thus, it is evident that the amendment to the claims conforms to the requirements of §112, first paragraph.

Claim 45 was added in the previous amendment. This claim includes a polypeptide having at least 95% identity along its entire length to the complete polypeptide of the amino acid sequence set forth in SEQ ID NO: 2. It has now been placed in independent form. Such claim scope was indicated in the Office action as having a written description and also to conform to the enablement requirements. See, e.g., Office action dated October 14, 2005, e.g., Page 5, lines 1-3; Page 10, lines 1-10. Yet, this claim stands rejected. Clarification is requested.

It is also evident that polypeptides with less sequence identity are enabled and supported by the written description of the patent specification. According to *University of California v. Eli Lilly*, 43 USPQ2d 1398, 1407 (Fed. Cir. 1997), as well as the PTO's own Written Description Guidelines, "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNA, defined by nucleotide sequence, falling within the scope of the

genus or of recitation of structural features common to the member of the genus." *Synopsis of Application of Written Description Guidelines*, Page 31. This would be similarly true for polypeptides. (Compare Example 8 on Page 33 of the *Guidelines*.) Thus, the question is whether an Applicant has provided a sufficient number of sequences to establish that they have possession of a genus of proteins that share structural features and/or conserved sequence identity. See, e.g., Guidelines, Page 33, line 14; Page 36, lines 19-21. In other words, do the sequences "represent" a genus of 70% or more sequence identity to which they are entitled to claim?

As argued in the Response filed August 25, 2004, the patent application specification describes the identification of ten different homologues of the BVH-P7 gene. See, e.g., Specification, Page 3, lines 14-20; Page 27, Table 2. These homologues show a high degree of sequence identity at the amino acid level and establish a structural framework to guide the skilled worker in making amino acid modifications. For example, Fig. 3 compares the amino acid sequences from seven different strains of S. pyogenes, showing the conserved motifs among the polypeptides. On Page 9, line 30-Page 10, line 14 of the specification, guidance is provided on what kinds of amino acid changes can be made, and includes the substitutions shown in Fig. 3. Taken together, it is clear that this information provides an adequate description of the claimed genus and sufficient guidance to enable the full scope of the claims.

The examples referred to in the Office action, e.g., fibroblast growth factor (e.g., Page 14) and EPO (Pages 15-17) are inapplicable because each of these are focused on a biological activity at a receptor site, where no structural features of the proteins were disclosed. Applicant has disclosed numerous species of BVH-P7, including conserved regions, and therefore clearly has shown possession of the claimed invention in its full breadth.

It is also alleged in the Office action that there is insufficient guidance for the purposes of §112, first paragraph, regarding fragments or epitopes that elicit antibodies specific for BVH-P7 of S. pyogenes. See, Office action, e.g., Page 7, lines 5-13; Page 10, 2nd paragraph. To the

contrary, the disclosure of the complete sequences of at least seven different homologues of BVH-P7 constitutes an adequate description since the skilled worker could clearly envision fragments of such sequences, especially in view of the disclosure which expressly identifies the concept of deriving fragment and epitopes from SEQ ID NO:2 and derivatives of it. The latter sequence, itself, is an express definition of all fragments within it. Thus, it is unclear what is deficient in terms of the written description requirement.

Fragments and epitopes that, e.g., elicit antibodies specific for BVH-P7 of S pyogenes, can be determined routinely. The standard for determining whether the claims are in compliance with the enablement requirement is whether it would require "undue experimentation" to make and use the claimed invention. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. In re Angstadt, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976). See, e.g., MPEP 2164.01. It would be routine for the skilled worker to take polypeptide fragments, e.g., of SEQ ID NO:2, and determine which fragments elicited antibodies specific for BVH-P7. Example 4 of the specification (beginning on Page 29) describes the production of recombinant proteins, thus further enabling the manufacture of polypeptide fragments. Examples 5 and 6 (beginning on Page 30) provide examples of immunization with polypeptides, and their ability to elicit antibodies. Reactivity is tested on immunoblots to show the antibody specificity. See, e.g., Table 3 on Page 31. It would be routine for a skilled worker, coupled with his knowledge, to utilize such disclosed methods to produce fragments and antibodies to these fragments, and to then determine the antibody binding specificity.

Rejection under §112, second paragraph

To clarify the issues raised by parts (f) and (g) of Claims 17, the claims have been amended and such aspects have been claimed in new Claims 46 and 47. Such amendment does not affect the claim scope, but merely clarifies the claimed subject matter.

In regard to Claim 42, stringent conditions were well known to the skilled worker on the application priority date, and are described in the specification as being readily determinable, especially in view of cited reference texts. See, Specification, Page 17, lines 26-32. "What is conventional or well known to one of ordinary skill in the art need not be disclosed in detail. See Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d at 1384, 231 USPQ at 94." See, M.P.E.P. §2163.

The claims recite that the claimed polypeptides have a certain amount of sequence identity to SEQ ID NO:2, and also that they possess an activity, i.e., elicit antibodies specific for BVH-P7. Such claim types have been indicated by the PTO and in *Enzo v Gen-Probe*, 285 F.3d 1013 (Fed. Cir. 2002) to comply with the written description requirements ("The PTO has also provided a contrasting example of genus claims to nucleic acids based on their hybridization properties, and has determined that such claims may be adequately described if they hybridize under highly stringent conditions to known sequences because such conditions dictate that all species within the genus will be structurally similar. See id., Example 9, at 35-37. ... On remand, the district court should determine, consistently with the precedent of this court and the PTO's Guidelines ... ").

Rejections under §102

Dixon et al. and McDonald et al., which are PIR database entries, are stated to anticipate certain aspects of the claims, allegedly because short regions of the disclosed polypeptides share sequence identity with the claimed polypeptides. However, there is no disclosure in these cited PIR database entries of **fragments** which contain the alleged regions of sequence identity. Only full-length polypeptides are disclosed in the database entries. Such disclosure is insufficient to anticipate those aspects of the claims that relate to, e.g., fragments and epitopes. Moreover, the cited database entries do not disclose fragments or epitopes of having 100% identity over at least ten contiguous amino acids.

The rejection under Section 102(a) over Ferretti et al., *Proc. Natl. Acad. Sci.*, 98: 4658-4663 is improper. As mentioned above, the priority document U.S. Serial. No. 60/269,840 discloses SEQ ID NO: 2. This priority application was filed February 21, 2001, which is prior to the April 10, 2001 publication date alleged in the Office action. (Applicant has not independently confirmed this publication date). Thus, it is not prior art under Section 102(a) and the rejection should be withdrawn.

Similarly, WO 01/32882 is cited as allegedly anticipating certain claims because of its publication on May 19, 2001. The priority document (U.S. Serial. No. 60/269,840) for the pending application was filed February 21, 2001, prior to the WO publication date, and therefore the cited WO is not prior art under Section 102(a). Consequently, this rejection should be withdrawn.

In view of the above remarks, favorable reconsideration is courteously requested. If there are any remaining issues which could be expedited by a telephone conference, the Examiner is courteously invited to telephone counsel at the number indicated below.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

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Attorney Docket No.: IDB-0018
Date: April 14, 2006